Filing Date:

Application No.:

Title:

Steven P. Adams et al.

CELL ADHESION INHIBITORS

10/625,626

July 24, 2003

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Amendments to the claims

This listing of claims will replace all prior versions and listings of the claims.

Listing of Claims:

1. (Currently amended) A cell adhesion inhibitory compound of formula (I):

$$R_1$$
 R_2
 R_3
 R_4
 R_4
 R_4
 R_4
 R_4

or a pharmaceutically acceptable salt thereof, wherein:

X is selected from the group consisting of $-CO_2H$, $-SO_2R_5$, and $-SO_3H$;

R₁ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkyl-substituted alkyl, cycloalkenyl-substituted cycloalkyl, alkoxy, alkenoxy, alkynoxy, alkylamino, alkenylamino, alkynylamino, N-alkylurea-substituted alkyl, alkylcarbonylamino-substituted alkyl, and aminocarbonyl-substituted alkyl;

R₂ is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl;

R₃ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, hydroxy-substituted alkyl, alkoxy-substituted alkyl, amino-substituted alkyl, thiol-substituted alkyl, alkylsulfonyl-substituted alkyl, (hydroxy-substituted alkylthio)-substituted alkyl, thioalkoxy-substituted alkyl, acylamino-substituted alkyl, alkylsulfonylamino-substituted alkyl, (N-(alkyl, alkenyl or alkynyl) or N,N-(dialkyl, dialkenyl, dialkynyl or (alkyl, alkenyl)-amino)carbonyl-substituted alkyl, carboxyl-substituted alkyl, and amino acid side chains selected from arginine, asparagine, glutamine, S-methyl cysteine, methionine and corresponding sulfoxide and sulfone derivatives thereof, glycine, leucine, isoleucine, allo-isoleucine, tert-leucine, norleucine, alanine, ornithine, glutamine, valine, threonine, serine, aspartic acid, beta-cyanoalanine, and allothreonine;

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R₄ is selected from the group consisting of alkyl, cycloalkyl, alkenyl, cycloalkenyl, and alkynyl;

R₅ is alkyl, alkenyl, cycloalkyl, cycloalkenyl, or alkynyl; and n is 0, 1 or 2.

- 2. (Original) The cell adhesion inhibitory compound according to claim 1, wherein R_1 is selected from the group consisting of cyanomethyl, cyclohexylmethyl, methyl, n-hexyl, t-butoxy, t-butylamino, 5-(N'-t-butylurea)pentyl, and 2,2-dimethylpropyl.
- 3. (Original) The cell adhesion inhibitory compound according to claim 1, wherein R₂ is hydrogen or methyl.
- 4. (Original) The cell adhesion inhibitory compound according to claim 3, wherein R₂ is hydrogen.
- 5. (Original) The cell adhesion inhibitory compound according to claim 1, wherein R₃ is selected from the group consisting of 2-(methylsulfonyl)-ethyl, 3-(hydroxy-propylthio)-methyl, 4-(methylsulfonylamino)-butyl, 4-acetylaminobutyl, aminomethyl, butyl, hydroxymethyl, isobutyl, methyl, methylthiomethyl, propyl, N,N-(methylpropargyl)-amino, 2-(methylthio)-ethyl, 2-(N,N-dimethylamino)-ethyl, 4-amino-butyl, t-butoxy-carbonylaminomethyl, sec-butyl, t-butyl, N,N-dimethyl-aminocarbonylmethyl, 1,1-ethano, 1-hydroxyethyl, 1-methoxyethyl, carbonylmethyl, 2-methylsulfinylethyl, and asparagine side-chain.
- 6. (Original) The cell adhesion inhibitory compound according to claim 5, wherein R₃ is selected from the group consisting of isobutyl, 2-(methylthio)-ethyl, 3-(hydroxypropylthio)-methyl, 2-(methylsulfonyl)-ethyl and 4-acetylamino-butyl, 4-(methylsulfonylamino)-butyl.
- 7. (Original) The cell adhesion inhibitory compound according to claim 1, wherein R₄ is methyl.

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8. (Cancelled)

- 9. (Currently amended) The cell adhesion inhibitory compound according to elaim 8 claim 1, wherein Y is -CO-.
- 10. (Original) The cell adhesion inhibitory compound according to claim 1, wherein n is 1.
- 11. (Currently amended) A pharmaceutical composition comprising a cell adhesion inhibitory compound of formula (I):

$$R_1 \xrightarrow{R_2} O \xrightarrow{I} R_4$$

$$R_3 \qquad (I)$$

or a pharmaceutically acceptable salt thereof, wherein:

X is selected from the group consisting of -CO₂H, $-SO_2R_5$, and $-SO_3H$;

R₁ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkyl-substituted alkyl, cycloalkenyl-substituted cycloalkyl, alkoxy, alkenoxy, alkynoxy, alkylamino, alkenylamino, alkynylamino, N-alkylurea-substituted alkyl, alkylcarbonylamino-substituted alkyl, and aminocarbonyl-substituted alkyl;

R₂ is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl;

R₃ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, hydroxy-substituted alkyl, alkoxy-substituted alkyl, amino-substituted alkyl, thiol-substituted alkyl, alkylsulfonyl-substituted alkyl, (hydroxy-substituted alkylthio)-substituted alkyl, thioalkoxy-substituted alkyl, acylamino-substituted alkyl, alkylsulfonylamino-substituted alkyl, (N-(alkyl, alkenyl or alkynyl) or N,N-(dialkyl, dialkenyl,

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dialkynyl or (alkyl, alkenyl)-amino)carbonyl-substituted alkyl, carboxyl-substituted alkyl, and amino acid side chains selected from arginine, asparagine, glutamine, S-methyl cysteine, methionine and corresponding sulfoxide and sulfone derivatives thereof, glycine, leucine, isoleucine, allo-isoleucine, tert-leucine, norleucine, alanine, ornithine, glutamine, valine, threonine, serine, aspartic acid, beta-cyanoalanine, and allothreonine;

R₄ is selected from the group consisting of alkyl, cycloalkyl, alkenyl, cycloalkenyl, and alkynyl;

R₅ is alkyl, alkenyl, cycloalkyl, cycloalkenyl, or alkynyl; and

n is 0, 1 or 2;

in an amount effective for prevention, inhibition or suppression of cell adhesion; and a pharmaceutically acceptable carrier.

12. (Currently amended) A method of preventing, inhibiting or suppressing cell adhesion in a mammal <u>in need thereof</u> comprising the step of administering to said mammal a pharmaceutical composition comprising an effective amount of a cell adhesion inhibitory compound of formula (I):

$$R_1$$
 R_2
 R_3
 R_4
 R_4
 R_4
 R_4

or a pharmaceutically acceptable salt thereof, wherein:

X is selected from the group consisting of - CO_2H , - SO_2R_5 , and - SO_3H ;

R₁ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkenyl, cycloalkenyl-substituted cycloalkyl, alkoxy, alkenoxy, alkynoxy, alkylamino, alkenylamino, alkynylamino, N-alkylurea-substituted alkyl, alkylcarbonylamino-substituted alkyl, and aminocarbonyl-substituted alkyl;

R₂ is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl;

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R₃ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, hydroxy-substituted alkyl, alkoxy-substituted alkyl, amino-substituted alkyl, thiol-substituted alkyl, alkylsulfonyl-substituted alkyl, (hydroxy-substituted alkyl, acylamino-substituted alkyl, alkylsulfonylamino-substituted alkyl, (N-(alkyl, alkenyl) or alkynyl) or N,N-(dialkyl, dialkenyl, dialkynyl or (alkyl, alkenyl)-amino)carbonyl-substituted alkyl, carboxyl-substituted alkyl, and amino acid side chains selected from arginine, asparagine, glutamine, S-methyl cysteine, methionine and corresponding sulfoxide and sulfone derivatives thereof, glycine, leucine, isoleucine, allo-isoleucine, tert-leucine, norleucine, alanine, ornithine, glutamine, valine, threonine, serine, aspartic acid, beta-cyanoalanine, and allothreonine;

R₄ is selected from the group consisting of alkyl, cycloalkyl, alkenyl, cycloalkenyl, and alkynyl;

R₅ is alkyl, alkenyl, cycloalkyl, cycloalkenyl, or alkynyl; and

n is 0, 1 or 2;

and a pharmaceutically acceptable carrier.

- 13. (Original) The method according to claim 12 wherein said method is used for preventing, inhibiting or suppressing cell adhesion-associated inflammation.
- 14. (Original) The method according to claim 12, wherein said method is used for preventing, inhibiting or suppressing a cell adhesion-associated immune or autoimmune response.
- 15. (Original) The method according to claim 12, wherein said method is used to treat or prevent a disease selected from the group consisting of asthma, arthritis, psoriasis, transplantation rejection, multiple sclerosis, diabetes and inflammatory bowel disease.